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Definitions

Pulmonary hypertension (PH) is defined as elevated pulmonary artery pressure (PAP) secondary to various pathophysiologies causing cor pulmonale and eventually right sided heart failure. The WHO classification of PH is based on similarities in pathophysiologic mechanisms (see table below). Specific hemodynamic criteria include systolic PAP >30 mmHg, diastolic PAP >20 mmHg, mean PAP >25 mmHg, pulmonary capillary wedge pressure <15 mmHg.

Pulmonary arterial hypertension (PAH) is a progressive vasoproliferative condition characterized by increased pulmonary artery pressure. Patients with PAH by definition do not have significant left heart disease, lung disease or chronic thromboembolic disease. Idiopathic PAH (formerly primary PH or PPH) is diagnosed, when no underlying cause for PH and characteristic histological abnormalities in small pulmonary arteries can be identified. Histological abnormalities include intimal, medial and adventitial proliferation, plexogenic changes consisting of proliferating epithelial cells mixed with myofibroblasts and necrotizing arteritis.

Cor pulmonale refers to right ventricular hypertrophy secondary to PH.

Etiology and pathophysiology

In PAH, the underlying vascular injury is thought to be a final common response to various inciting factors coupled with genetic susceptibility. Eliciting factors may be mechanical (overperfusion), drugs (experimentally inducible with appetite suppressants), toxins, infections, and genetically determined susceptibility to such injuries. Thrombosis elicited by diseased vessel walls may complicate PAH.

PH is a common complication of different cardiac and extracardiac diseases and results from two main mechanisms: increased left atrial pressure and increased pulmonary vascular resistance. Important causes are

Cardiac: Pulmonary venous hypertension due to increased left atrial pressure in left myocardial failure, most common in advanced chronic mitral regurgitation, also in dilated cardiomyopathy; cor triatriatum sinister, mitral stenosis.

Hypoxic vasoconstriction: Chronic obstructive lower airway disease (bronchitis, emphysema); chronic obstructive upper airway disease; high altitude hypoxia
Occlusion of the pulmonary vascular bed: PTE; Parasites (*D. immitis, A. vasorum*),
Pulmonary parenchymal disease: Pulmonary fibrosis; ARDS
Combination of mechanisms, e.g., heartworm infection (*D. immitis, A. vasorum*): obstruction by intravascular parasites, vasculitis, thrombosis, and hypoxic vasoconstriction.

Table: Classification of pulmonary hypertension*

Group 1. Pulmonary arterial hypertension (PAH)
Idiopathic (formerly primary PH, PPH)
Associated with congenital systemic-to-pulmonic shunts
Persistent pulmonary hypertension of the newborn
Associated with drugs, toxins, inflammatory conditions

Group 2. Pulmonary hypertension associated with left heart disease
Left ventricular or atrial disease
Left-sided valvular disease

Group 3. Pulmonary hypertension associated with respiratory disease and/or hypoxemia
Interstitial lung disease, e.g. pulmonary fibrosis
Chronic upper airway obstruction
Chronic exposure to high altitude

Group 4. Pulmonary hypertension due to thromboembolic disease
Primary cardio-vascular lesion, e.g. *D. immitis, A. vasorum*
Medical condition predisposing to pulmonary thromboembolism

Group 5. Miscellaneous

*source: WHO classification, Chin and Rubin, 2008, modified and adapted for dog

Diagnosis

Thoracic radiographs for signs of PH as well as potential underlying cause of PH. Dorsoventral view particularly helpful to document right ventricular and main pulmonary artery enlargement. Peripheral pulmonary vasculature may be tortuous and enlarged.

Left atrium is enlarged and pulmonary veins are congested with underlying left atrial, ventricular or mitral valve disease.

Signs of underlying bronchial, interstitial or alveolar pulmonary disease may be evident.

Echocardiogram, dual role:

Rule in or out causes of PH, including acquired left ventricular heart disease (mitral endocardiosis, dilated cardiomyopathy) and congenital cardiovascular shunt.

Confirmation of PH qualitatively and quantitatively:

Qualitatively: characteristic two-dimensional and M-mode findings in moderate to severe PH are dilation of right ventricle and atrium, thickening of right ventricular wall and papillary muscles, paradoxical septal motion, and decreased left ventricular chamber size.

Quantitatively: Doppler examination is the most useful noninvasive clinical tool to confirm and quantitate severity of PH. Systolic: velocity of tricuspid regurgitation (TR) correlates to right ventricular systolic pressure, and therefore, barring pulmonic stenosis, to pulmonary arterial systolic pressure. The modified Bernoulli equation allows Doppler-derived blood flow velocities to be used for estimating intracardiac pressures: $PG = 4 \times (Vmax)2$, where PG is the peak pressure gradient between right ventricle and right atrium, in mmHg, and Vmax is the peak velocity of tricuspid regurgitation (TR), in m/sec. It is assumed that right atrial pressure approximates 0 mmHg during ventricular systole, such that the right atrial:right ventricular systolic PG equals systolic right ventricular pressure. A TR-PG >30 mmHg (Vmax >2.8 m/s) suggests/indicates systolic PH. Diastolic pulmonary artery pressure is calculated with Doppler quantification of pulmonary valve insufficiency (PI) instead of tricuspid regurgitation; by this method PH is considered to be present when PI-PG is >20 mmHg (Vmax >2.2 m/s).

Advanced or confirmatory testing

Contrast ultrasound (microbubbles) of the heart and descending aorta to rule out cardiovascular right-to-left shunt. Shunt is also possible due to pulmonary arteriovenous fistula secondary to pulmonary hypertension; in this case, bubbles will take at least 3

cardiac cycles from their appearance in the right atrium till their appearance in the left atrium.

Right-sided cardiac catheterization for invasive measurement of pulmonary wedge pressure as an estimate of left atrial pressure, systolic and diastolic pulmonary artery pressure; evaluation of therapeutic intervention

Pulmonary angiography; tortuous pulmonary arteries indicate PH, perfusion deficits are present in PTE

Pulmonary Computed Tomography (CT) to identify / rule-out parenchymal disease and Angio-CT for PTE.

Pulmonary ventilation-perfusion scintigraphy to rule out PTE

Pulmonary histopathologic evaluation to confirm PAH

Therapeutic goals

PH of any genesis with signs referable to right ventricular forward or backward failure: lower pulmonary artery pressure

PH of any genesis with signs referable to hypoxia: improve oxygenation

PH with known pathogenesis and treatable cause: focus should be to correct/improve underlying disease

There is no randomized trial documenting efficacy of medical treatment in naturally occurring PH in dogs; thus the following are merely treatment considerations:

Therapeutic trial with amlodipine (Norvasc) in moderate PH, starting at 0.05 mg/kg PO q 24h and titrating dose based on response and BP (avoid hypotension)

Anticoagulant therapy with low dose aspirin, 2–5 mg/kg PO q 12h (dog)

Sildenafil (Viagra) in severe PH, 2–3 mg/kg PO q 8-12h. Improves clinical condition in the absence of significant effects on PAP as estimated by TR-PG.

Oral L-Arginine, a precursor of nitric oxide, may be a simple and useful oral medical treatment, however, no studies documenting effect.

Dedicated owner may consider intermittent oxygen therapy at home

Pimobendan may lower PAP

Furosemide, ACE inhibitor, spironolactone in case of overt right-sided congestive heart failure.

Specific treatment of underlying mechanism or disease in secondary PH (Heart Failure, Pulmonary Thromboembolism, Dirofilariosis, Angiostrongylosis)

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